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EXAMINER	
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ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
09/25/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docketing@mwzb.com

Office Action Summary	Application No.	Applicant(s)	
	10/518,927	FIEBIG ET AL.	
	Examiner	Art Unit	
	NORA M. ROONEY	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13,15,16,20-22,25-33,35 and 36* is/are pending in the application.

4a) Of the above claim(s) *1-12 and 16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13,15,20-22,25-33,35 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 03/18/2009 has been entered.

2. Applicant's amendment and election of the polypeptide variant of the sequence set forth in SEQ ID NO: 2 with the amino acid variations set forth in clone1, comprising, L54, 157, V62, S76, T100, N107, Y137, P141, T142, K189, Q219, K221, L227, 1231, S235, T237, V238, K248, A258, 1264, K270, K282, L287, P299, A321, L322, S332, Q346, P347, T351, L357, N358, V362, S384, A410, D419, Y456, A457, K460, and E472 filed on 06/29/2009 is acknowledged.

3. Claims 1-13, 15-16, 20-22, 25-33 and 35-36 are pending.

4. Claims 1-12 and 16 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Groups, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 06/29/2007.

5. Claims 13, 15, 20-22, 25-33 and 35-36 are currently under examination as they read on a polypeptide encoded by the nucleic acid sequence of SEQ ID NO:1 and a pharmaceutical composition or vaccine thereof.

Claim Objections

6. Claims 13 and 26 are objected to because of the following informalities:

In claim 13, lines 8-29, the letter designations a-k should be changed to numeric designations for clarity, as was done in claim 22. The two (a), (b) and (c) designations in claim 13 makes claim 26 unclear.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 15, 20-22, 25-32 and 35-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for: recombinant, isolated polypeptides of SEQ ID NO: 2, 4, 6 encoded by SEQ ID NO:1, 3 or 5, respectively, the variants of SEQ ID NO:2 in clones 1-11, the polypeptide fragments 1-200 and 185-500 thereof and a composition thereof, does not reasonably provide enablement for: a **pharmaceutical composition** comprising at least

one polypeptide according to Claims 13 or 21-23 of claims 15 and 30-32; an **immunotherapeutic vaccine** comprising a polypeptide of Claims 13 or 21-23 and an acceptable carrier, wherein said **vaccine is capable of generating an immunomodulatory, T-cell response in a host** of claims 20 and 27-29 and **which is capable of generating a hypoallergenic action in the host** of claim 25; an **immunomodulatory, T-cell-reactive polypeptide fragment which comprises a partial sequence of 50 to 350 amino acids** of the polypeptide sequence (set forth in of claim 13) of claim 21; and wherein each of the polypeptides (of claim 13) **is immunogenic and induces an immunomodulatory T-cell reactive response in a host** of claim 26. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for the same reasons as set forth in the Office Action mailed on 09/18/2008.

Applicant's arguments filed on 03/18/2009 have been fully considered, but are not found persuasive.

Applicant argues:

> "Based on the Examiner's statement in the paragraph bridging pages 9 and 10 of the Office Action, further in view of the forgoing amendments, it is submitted that the alleged lack of enablement, at least with respect to the structure of the claimed polypeptides, is moot. Applicants' claims are directed to polypeptide molecules and fragments thereof comprising specific sequences. Variants of the claimed molecules, comprising, for example, the amino acid variations at the recited position in the polypeptide sequence of SEQ ID NO:2, are further disclosed. The detailed disclosure contained in Applicants' specification (as substantiated by the disclosure of three polypeptide sequences and 11 other clonal variants) provides a detailed description of the structure/activity of the claimed variant sequences and fragments. See also, the sequence listing page and the tables. The biological activities of such polypeptide molecules, for example, with respect to their reactivity to IgE molecules, are further disclosed. See, the disclosure in Fig. 5 and the description thereof at page 6 of the present application.
>
> Claims directed to the pharmaceutical composition/vaccines
>
> In the paragraphs bridging pages 11 and 12, the Office Action alleges that the pharmaceutical compositions and/or vaccines of the present invention are non-enabled. This contention is respectfully traversed.

At the outset, Applicants courteously submit that the Office Action fails to present any evidence which suggests the pharmaceutical compositions, as claimed herein, are not enabled. In the absence of such evidence, the rejection is deficient under controlling case law.

The burden is upon the Patent and Trademark Office to provide evidence shedding doubt that the invention can not be made and used as stated; see for example, In re Marzocchi, 439, F. 2d 220, 169 USPQ 367 (CCPA 1971). Moreover, Applicants' specification teaches that molecules of the present invention are useful formulation of vaccines and/or pharmaceutical compositions. See the generic teachings offered in the paragraph bridging page 15 and 16 of the present In relation to a disclosure on the utilization of Phi p 4 polypeptides as a pharmaceutical composition, the Examiner is courteously invited to review the disclosure contained in the Examples of the present application. See, for example, the paragraphs bridging page 7, line 28 to page 8, line 24 of the instant specification, as originally filed. In this regard, Applicants' specification expressly teaches that fragment and/or recombinant forms of allergens, which exhibit a different IgE reactivity profile compared to the natural allergen (nPhi p 4), can be utilized as pharmaceutical compositions or vaccines. Rationale for the use of the molecules of the instant invention in the desensitization of a subject suffering from allergy is also provided. See, the page 15, lines 9-27; page 16, lines 19-24 of the specification, as originally filed.

Moreover, the disclosure in page 8, lines 3-17 of Applicants' specification and the cited Schramm reference expressly teach that the use of hypoallergenic peptide molecules, such as the rPhi p 4 variant polypeptide of the present invention, for therapy of allergic diseases was appreciated by one of ordinary skilled in the art. To this end, the Examiner is also cordially requested to review the entirety of disclosure contained in the cited reference of Fischer et al. (Journal of Allergy and Clinical Immunology, 1996). Also enclosed is a scientific article by Focke et al. (FASEB Journal, vol. 15, 2042-44, 2001). As evidenced by the disclosure in the Focke et al., it is respectfully submitted that as of the filing date of the present application, the instantly claimed grass pollen allergens could be routinely manipulated and utilized as pharmaceutical preparations in a manner recited in the claims.

In the last paragraph at page 12, the Office Action alleges that it would "the experimentation left to those skilled in the art is unnecessarily and improperly, extensive and undue." These allegations, however, do not present any evidence to doubt the objective enablement of Applicants' disclosure. As clearly and succinctly stated by the court in Iv *re Marzocchi*, 169 USPQ 367, 369 (CCPA 1971):

As a matter of Patent Office practice, then a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken in compliance with the enabling requirement of the first paragraph of 5112, unless there is reason to doubt the objective truth of statements contained therein relied on for enabling support. (emphasis in original)

Furthermore, as stated in *Marzocchi*, at 370, the PTO must have adequate support (evidence or reasoning) for its challenge to the credibility of Appellants' statements ofenablement. Thus, in the absence of evidence which demonstrates otherwise, the claims must be taken to satisfy the requirements of 35 U.S.C. 112, ¶1. Working examples are not required to establish enablement. As stated by the court *Marzocchi*, at page 369:

The first paragraph of 5112 requires nothing more than objective enablement. How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance.

The assertion of undue experimentation in the rejection is merely conclusory. Further, as discussed above, the specification provides more than sufficient guidance to make and use the claimed vaccines and/or pharmaceutical compositions using no more than routine experimentation. Finally, a high level of skill does not establish that one skilled in the art would have reasons to doubt the veracity of the statements in Applicants' specification with respect to the use of the claimed composition in the diagnosis, treatment, and/or prevention of the claimed conditions.

> Based on the aforementioned remarks and arguments, further in view of the amendments presented herein, it is respectfully submitted that Applicants' specification provides an enabling disclosure of what is claimed by the present invention. Withdrawal of the rejection under 35 U.S.C. 5112, ¶1, is respectfully requested."

It is the Examiner's position that when a compound or composition claim is limited by a particular use, enablement of that claim should be evaluated based on that use. See MPEP 2164.01(c). Following the guidance from the MPEP, for the claim to be enabled, the specification must teach how to make the claimed composition without undue experimentation and must teach how to use the composition for at least one pharmaceutical use without undue experimentation. According to Steadman's Medical Dictionary (24th Edition, 1982), "pharmaceutical" means "relating to pharmacy or to pharmaceutics". In the same dictionary, "pharmacy" is defined as: 1.The practice of preparing and dispensing drugs. 2. A drugstore. and "clinical" is defined as a branch of practice that emphasizes the therapeutic use of drugs rather than the preparation and dispensing of drugs. Thus, broadly speaking, unless defined otherwise in the specification, a "pharmaceutical use" would be one wherein something is being used as a "drug". Steadman's Medical Dictionary (24th Edition, 1982) defines "drug" as "A therapeutic agent; any substance, other than food, used in the prevention, diagnosis, alleviation, treatment, or cure of disease in man and animal." Therefore, a pharmaceutical use would be any use, other than as food, wherein a substance is used on or in the body to prevent, diagnose, alleviate, treat, or cure a disease in humans or animals. However, such a definition is not so broad as to cover *any* use of a substance on or in the body of a human or animal, only those uses intended to prevent, diagnose, alleviate, treat, or cure a disease within the animal to which the substance was administered. Thus, to enable a pharmaceutical use for a substance, the

specification must teach how to use the substance, without undue experimentation, for the prevention, diagnosis, alleviation, treatment, or cure a disease in the animal to which the substance is administered. When applicant is claiming a pharmaceutical composition, applicant must enable a pharmaceutical use. This rejection could be overcome by deleting the words "pharmaceutical" and "vaccine" from the claim as when no use is recited in a claim, any enabled use will suffice.

The claims, as recited, include the use of SEQ ID NOs: 2, 4, or 6, the variants of SEQ ID NO:2 in clones 1-11, any polypeptide comprising amino acids 1-200, amino acids 185-500 and any 50 to 350 amino acid long peptide from SEQ ID NO: 2, 4, 6 or the variants of SEQ ID NO:2 in clones 1-11. It is well known in the art that even small changes can affect the binding specificity of an antibody. Colman *et al.* (PTO-892 Reference U) teaches that single amino acid changes in an antigen can effectively abolish antibody antigen binding. Abaza et al. in (PTO-892; Reference V) teaches that single amino acid substitutions that are outside the antigenic site on a protein effect antibody binding. Further, Lederman *et al.* (PTO-892 Reference W) disclose that a single amino acid substitution in a common allele ablates binding of a monoclonal antibody (see entire document). In addition, Blumenthal et al. teaches that correlations between structure and IgE binding (or the lack of IgE binding) cannot be predicted on an a priori structural basis (PTO-892, Reference X, see entire document and page 39 of third full paragraph). Kinnunen et al. (PTO-892 page 2, Reference U, abstract, discussion) teaches that the use of allergen peptide derivatives or "altered peptide ligands" of the lipocalin allergen. The reference teaches that APL induce differential T cell stimulation (In particular, Table I, page 6, paragraph spanning left and right columns). The discussion cautions those who are looking to

use APL in immunotherapy for allergy because some T cells populations, such as pathogenic memory cells, that are induced by certain APL would exacerbate allergic disease (In particular, page 7, left column, second paragraph). One of ordinary skill in the art would be required to determine how alterations to each position of the peptide affect binding to MHC and how that in turn effects T cell activation. The T cell activation induced by the peptide in vivo would need to promote hypoallergenic/ tolerogenic effects, which is also highly unpredictable. In addition, the art of whole allergen immunotherapy as taught by Tarzi et al. (PTO-892 page 2; Reference V) teaches that whole allergen immunotherapy is unpredictable due to the retention of B-ell epitopes within the allergen which confers a risk of IgE-mediated potentially life-threatening systemic reactions (In particular, paragraph spanning pages 617-618, whole document). Therefore, it is unpredictable whether the natural whole allergen variants of SEQ ID NO:2, 4 and 6 could be used as pharmaceutical compositions and immunotherapeutic vaccines as well. The specification has not adequately disclosed the genus of allergens, variants and peptides thereof to be used to treat or prevent allergy or, as encompassed by the claimed invention. The aforementioned unpredictibility in the art highlights that an undue amount of experimentation is necessary to practice the claimed invention.

A vaccine is a composition to induce specific immunity that **prevents** or protects against a specific disease caused by a specific agent. The specification provides no information on the vaccine formulation comprising any polypeptide, derivative or fragment of SEQ ID NO:2, 4 or 6 or the variants of SEQ ID NO:2 in clones 1-11 which is able to exhibit antigen-specific antibody response, stimulated memory T lymphocytes and to protect or prevent against allergy. Vaccines by definition trigger an immunoprotective response in the host vaccinated and a mere antigenic

response is insufficient. The specification provides no in vivo data to support the claimed subject matter. The specification fails to provide guidance as to how to totally prevent (100% prevention) allergy using a vaccine or pharmaceutical composition encompassed by the instant claim recitations. It is possible that the compositions encompassed may reduce the likelihood of an allergy, but the specification does not disclose how to totally prevent allergy.

Therefore, for all the reasons stated *supra*, it remains at issue is whether or not the claimed compositions would function as a 'pharmaceutical composition' and/or 'immunotherapeutic vaccine.' In view of the absence of a specific and detailed description in Applicant's specification of how to effectively use the pharmaceutical composition or vaccine as claimed, absence of working examples providing evidence which is reasonably predictive that the claimed pharmaceutical compositions or vaccine are effective for in vivo use, and the lack of predictability in the art at the time the invention was made, an undue amount of experimentation would be required to practice the claimed pharmaceutical composition with a reasonable expectation of success.

The limitations of "an immunotherapeutic vaccine" and wherein "said vaccine is capable of generating an immunomodulatory, T-cell response in a host" of claims 20 and 27-29; "which is capable of generating a hypoallergenic action in the host" of claim 25; "an immunomodulatory, T-cell-reactive polypeptide fragment" of claim 21; and wherein the polypeptide is "immunogenic and induces an immunomodulatory T-cell reactive response in a host "of claim 26 are not seen as providing a requisite functional activity since numerous

functional activities are encompassed by the specification and claims. The term immunomodulatory implies that the immune system is changed, but no specific changes are recited. Therefore, the term 'immunomodulatory' encompasses just about any reaction by any cells or pathways related to the immune system. In the same way, the term 'T-cell reactive' is largely undefined. Any fragment or processed subsequence of the fragment that induces any T cell response or interaction is encompassed by the instant claims. The specification does not provide sufficient guidance as to which variants retain the requisite functions.

In addition, the specification does not provide support for any polypeptide fragments which "comprises a partial sequence of 50 to 350 amino acids." The term 'comprises' is open language which opens the claim up to encompass an enormous number of undisclosed fragments which may include sequence that is unrelated to the polypeptides of SEQ ID NO:2, 4 or 6 or the variants of SEQ ID NO:2 in clones 1-11 that could independently possess the requisite functions.

9. Claims 15, 20-22, 25-32 and 35-36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of : recombinant, isolated polypeptides of SEQ ID NO: 2, 4, 6 encoded by SEQ ID NO:1, 3 or 5, respectively, the variants of SEQ ID NO:2 in clones 1-11, the polypeptide fragments 1-200 and 185-500 thereof and a composition thereof

Applicant is not in possession of : a **pharmaceutical composition** comprising at least one polypeptide according to Claims 13 or 21-23 of claims 15 and 30-32; an **immunotherapeutic vaccine** comprising a polypeptide of Claims 13 or 21-23 and an acceptable carrier, wherein said **vaccine is capable of generating an immunomodulatory, T-cell response in a host** of claims 20 and 27-29 and **which is capable of generating a hypoallergenic action in the host** of claim 25; an **immunomodulatory, T-cell-reactive polypeptide fragment which comprises a partial sequence of 50 to 350 amino acids** of the polypeptide sequence (set forth in of claim 13) of claim 21; and wherein each of the polypeptides (of claim 13) **is immunogenic and induces an immunomodulatory T-cell reactive response in a host** of claim 26 for the same reasons as set forth in the Office Action mailed on 09/18/2008.

Applicant's arguments filed on 03/18/2009 have been fully considered, but are not found persuasive.

Applicant argues:

> "The contention that "the specification does not provide support for any polypeptide 'comprising' fragments of polypeptide of SEQ ID NOs: 2, 4, or 6 or variants of SEQ ID NO: 2 in clones 1-11" is respectfully traversed. Applicants' specification expressly teaches that Phl p4 polypeptide of the invention comprises polypeptides having the polypeptide sequence set forth in SEQ ID NOs: 2, 4, or 6 or variants of SEQ ID NO: 2 in clones 1-11. See, for example, paragraph [0042] of the published application and the disclosure contained in the Tables (with respect to the variant sequences). In the Examples section, two such Phl p 4 fragments corresponding to amino acids 1-200 and 185-500 of the Phl p4 polypeptides (SEQ

> ID NOs: 2, 4, and 6 each comprise 500 amino acid residues) are expressly described. Thus the structural information of at least six such fragment sequences (i.e., N-terminal and C-terminal fragments of SEQ ID NOs: 2, 4, and 6) are explicitly taught by the instant application. Other representative examples of such fragment sequences, for example, Pl-P6 (SEQ ID NOs: 27-32) obtained from the amino acid sequencing of the purified and fragmented Phi p 4 allergens are additionally described in the instant application. See also the sequence listing page. As such, the PTO's contentions that the fragment sequences lack adequate written description is without merit. Moerover, given the detailed disclosure in Applicants' specification, *any* fragment of the claimed polypeptide sequences can "at once be envisaged" by one of ordinary skill in the art. Explicit recitation of each and every sequence is not necessary at all. See, *In rePetering* 301 F.2d 676, 133 USPQ 275 (CCPA 1962). Withdrawal of the rejection is respectfully requested."

It is the Examiner's position that the specification has not adequately disclosed the genus of polypeptide variants fragment comprises a partial sequence of the disclosed polypeptides wherein the polypeptide fragments have a function (immunomodulatory and T-cell reactive), particularly when in the context of an immunotherapeutic vaccine or pharmaceutical composition. In addition, the disclosed genus of polypeptide fragments are not limited to true fragments of the disclosed sequences, but instead, may comprise additional sequence that can be responsible for the claimed and disclosed functions. Therefore, the term "comprises" may not be used except when claiming full-length sequences.

It is also the Examiner's position that the specification does not disclose a correlation structure of the allergens, variants and fragments thereof and function ("immunotherapeutic vaccine," " capable of generating an immunomodulatory, T-cell response in a host" of claims 20 and 27-29; "capable of generating a hypoallergenic action in the host" of claim 25; "immunomodulatory, T-cell-reactive" of claim 21; and "immunogenic and induces an immunomodulatory T-cell reactive response in a host "of claim 26) such that a skilled artisan would have known what allergen variants and fragments of the Phl p 4 allergens attain the claimed functions. "Possession may not be shown by merely describing how to obtain

possession of member of the claimed genus or how to identify their common structural features" *Ex parte Kubin* (83 U.S.P.Q.2d 1410 (BPAI 2007)), at page 16. In this instant case Applicants have not provided any guidance as to what variants and fragments will result in the claimed functions. "Without a correlation between structure and function, the claim does little more than define the claimed invention by function" *supra*, at page 17. Definition by function does not suffice to define the genus because it is only an indication of what the allergen does and what functional properties it has, rather than what it is.

Contrary to Applicant's assertion, the term comprises opens the claim up to encompass a genus of polypeptides that cannot be determined because the genus is limitless. The term comprises may only be used when one may determine the members of the genus encompassed. The exception to this requirement is when full-length polypeptides are claimed because a correlation between the structure of the polypeptide and the function is readily ascertainable. The written description guidelines are also not satisfied by the instant claim recitations because they include functions. The specification only satisfies the written description requirement when there is an established correlation between the structure and function.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 13, 15, 20-22, 25-33 and 35-36 are rejected under 35 U.S.C. 102(b) as being anticipated by Fischer et al. (PTO-892 mailed on 06/07/2007, Reference U) for the same reasons as set forth in the Office Action mailed on 09/18/2008.

Fischer et al teaches isolation of the allergen Phl p 4 from Phleum pratense in a pharmaceutically acceptable carrier (Tris-buffered saline or water) (In particular, 'Methods' section on pages 190-192, whole document).

The recitations of "which comprises the polypeptide sequence set forth in SEQ ID NO: 2, SEQ ID NO: 4 or SEQ ID NO: 6" and "which is encoded by a the polynucleotide sequence is set forth in SEQ ID NO: 1, SEQ ID NO: 3 or SEQ ID NO: 5" of claim 13; "comprises a partial sequence of 50 to 350 amino acids of the polypeptide" of SEQ ID NO:2 SEQ ID NO:4 or SEQ ID NO:6 of claim 21; which comprises "amino acids 1-200 of the polypeptide" or "amino acids 185-500 of the polypeptide" of SEQ ID NO:2 SEQ ID NO:4 or SEQ ID NO:6 of claim 22; which "comprises (a) a polypeptide which is encoded by single nucleotide polymorph of a polynucleotide whose sequence is set forth in SEQ ID NO: 1, (b) a single amino acid polymorph of a polypeptide whose sequence is set forth in SEQ ID NO: 2" of claim 33 is inherent. The reference Phl p 4 molecule is the same as the protein of claims. Further characterization of a known compound does not make it patentably distinct. See Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999) "Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art... However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's

functioning, does not render the old composition patentably new to the discoverer. " The Court further held that "this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art."

The recitations of "an immunotherapeutic vaccine" and wherein "said vaccine is capable of generating an immunomodulatory, T-cell response in a host" of claims 20 and 27-29; "which is capable of generating a hypoallergenic action in the host" of claim 25; "an immunomodulatory, T-cell-reactive polypeptide fragment which comprises a partial sequence of 50 to 350 amino acids" of claim 21; and wherein the polypeptide is "immunogenic and induces an immunomodulatory T-cell reactive response in a host "of claim 26 are inherent. Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced Phl p 4 allergen. Products of identical chemical composition cannot have mutually exclusive properties because a chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. Where the Patent Office has reason to believe that a functional limitation asserted to be critical for establishing novelty in the claimed subject matter may be an inherent characteristic of the prior art, it has the authority to require the applicant to prove that the subject matter shown in the prior art does not possess the characteristics relied on. In re Schreiber, 44 USPQ2d 1429 (Fed. Cir. 1997).

It is noted in the specification on page 14 that there are three natural isoforms of the heterogenous Phl p 4 allergen molecule (SEQ ID NOs 2, 4 and 6). Since the office does not have a laboratory to test the reference Phl p 4 allergen, it is applicant's burden to show that the reference allergen does not comprise the amino acid sequences of SEQ ID NO:2, 4 and 6 recited in the claims. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980).

Applicant's arguments filed on 03/18/2009 have been fully considered, but are not found persuasive.

Applicant argues:

> " Fischer teaches decapeptide sequence of Phl p 4 containing ten amino acid residues (IVALPXGMLK) of the N-terminal region of Phl p 4. See, Fig. 5 and the description thereof at page 194 of Fischer et al. Fischer fails to teach or suggest the polypeptides of the present invention, for example, a polypeptides which comprise the sequences set forth in SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6, or a variant of the sequence set forth in SEQ ID NO: 2, with the amino acid variations set forth in clones 1-11. Moreover, the cited reference fails to disclose the structural elements of the claimed fragments, comprising, for example, 50-350 amino acid residues. See, amended claim 21. Absent such, the reference cannot anticipate what is claimed herein."

It is the Examiner's position that the decapeptide taught by Fisher et al is not necessary to anticipate the instant claims because the reference need not teach the polypeptide sequence at all to anticipate the instant claims. Further characterization of a known compound does not make it patentably distinct. See Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999) "Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art... However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. " The Court further held that "this same reasoning

holds true when it is not a property but an ingredient which is inherently contained in the prior art." It is Applicant's burden to prove that the reference Phl p 4 molecule, which was isolated from the same source as the claimed Phl p 4 allergen, does not have the sequence of SEQ ID NO:2, 4 or 6. Where the Patent Office has reason to believe that a functional limitation asserted to be critical for establishing novelty in the claimed subject matter may be an inherent characteristic of the prior art, it has the authority to require the applicant to prove that the subject matter shown in the prior art does not possess the characteristics relied on. In re Schreiber, 44 USPQ2d 1429 (Fed. Cir. 1997).

12. Claims 13, 15, 20-22, 25-33 and 35-36 are rejected under 35 U.S.C. 102(b) as being anticipated by Suck et al. (Reference 4; IDS filed 12/23/2004) for the same reasons as set forth in the Office Action mailed on 09/18/2008.

Suck et al teaches isolated Phl p 4 from Phleum pratense in a pharmaceutically acceptable carrier (water) (In particular, 'Materials and Methods' section on page 1396, Figure 4, whole document).

The recitations of "which comprises the polypeptide sequence set forth in SEQ ID NO: 2, SEQ ID NO: 4 or SEQ ID NO: 6" and "which is encoded by a the polynucleotide sequence is set forth in SEQ ID NO: 1, SEQ ID NO: 3 or SEQ ID NO: 5" of claim 13; "comprises a partial sequence of 50 to 350 amino acids of the polypeptide" of SEQ ID NO:2 SEQ ID NO:4 or SEQ ID NO:6 of claim 21; which comprises "amino acids 1-200 of the polypeptide" or "amino acids 185-500 of the polypeptide" of SEQ ID NO:2 SEQ ID NO:4 or SEQ ID NO:6 of claim 22; which "comprises (a) a polypeptide which is encoded by single nucleotide polymorph of a

polynucleotide whose sequence is set forth in SEQ ID NO: 1, (b) a single amino acid polymorph of a polypeptide whose sequence is set forth in SEQ ID NO: 2" of claim 33 is inherent. The reference Phl p 4 molecule is the same as the protein of claims. Further characterization of a known compound does not make it patentably distinct. See Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999) "Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art... However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. " The Court further held that "this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art."

The recitations of "an immunotherapeutic vaccine" and wherein "said vaccine is capable of generating an immunomodulatory, T-cell response in a host" of claims 20 and 27-29; "which is capable of generating a hypoallergenic action in the host" of claim 25; "an immunomodulatory, T-cell-reactive polypeptide fragment which comprises a partial sequence of 50 to 350 amino acids" of claim 21; and wherein the polypeptide is "immunogenic and induces an immunomodulatory T-cell reactive response in a host "of claim 26 are inherent. Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced Phl p 4 allergen. Products of identical chemical composition cannot have mutually exclusive properties because a chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims

are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. Where the Patent Office has reason to believe that a functional limitation asserted to be critical for establishing novelty in the claimed subject matter may be an inherent characteristic of the prior art, it has the authority to require the applicant to prove that the subject matter shown in the prior art does not possess the characteristics relied on. In re Schreiber, 44 USPQ2d 1429 (Fed. Cir. 1997).

It is noted in the specification on page 14 that there are three natural isoforms of the heterogenous Phl p 4 allergen molecule (SEQ ID NOs 2, 4 and 6). Since the office does not have a laboratory to test the reference Phl p 4 allergen, it is applicant's burden to show that the reference allergen does not comprise the amino acid sequences of SEQ ID NO:2, 4 and 6 recited in the claims. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980).

Applicant's arguments filed on 03/18/2009 have been fully considered, but are not found persuasive.

Applicant argues:

> "Based on the Examiner's rationale at page 31 of the Office Action, it appears that this rejection is based on the cited references' disclosure of the term Phl p 4 polypeptide. The Office Action has not established that such polypeptides are structurally and/or identical to the claimed polypeptide(s) of the present invention. More specifically, the totality of the disclosure in Fisher, Suck and Fahlbusch says nothing about the identity of the polypeptides having the sequences set forth in SEQ ID NO: 2, 4, or 6 or clones 1-11 ofSEQ ID NO: 2, or the specific fragments of said polypeptides. Absent such, the reference(s) cannot anticipate what is claimed herein. It is required that for anticipation, the reference(s) explicitly or inherently disclose the claimed subject matter. See also new claims 35 and 36."

Contrary to Applicant's assertion, Suck et al. need not teach the polypeptide sequence to anticipate the instant claims. Further characterization of a known compound does not make it patentably distinct. See Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999) "Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art... However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. " The Court further held that "this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art." Therefore, it is Applicant's burden to prove that the reference Phl p 4 molecule, which was isolated from the same source as the claimed Phl p 4 allergen, does not have the sequence of SEQ ID NO:2, 4 or 6. Where the Patent Office has reason to believe that a functional limitation asserted to be critical for establishing novelty in the claimed subject matter may be an inherent characteristic of the prior art, it has the authority to require the applicant to prove that the subject matter shown in the prior art does not possess the characteristics relied on. In re Schreiber, 44 USPQ2d 1429 (Fed. Cir. 1997).

13. Claims 13, 15, 20-22, 25-33 and 35-36 are rejected under 35 U.S.C. 102(b) as being anticipated by Fahlbusch et al. (Reference 3; IDS filed on 12/23/2004) for the same reasons as set forth in the Office Action mailed on 09/18/2008.

Fahlbusch et al teaches isolated Phl p 4 from Phleum pratense in a pharmaceutically acceptable carrier (water) (In particular, 'Methods' section; paragraph spanning pages 801-802, Figure 1; whole document).

The recitations of "which comprises the polypeptide sequence set forth in SEQ ID NO: 2, SEQ ID NO: 4 or SEQ ID NO: 6" and "which is encoded by a the polynucleotide sequence is set forth in SEQ ID NO: 1, SEQ ID NO: 3 or SEQ ID NO: 5" of claim 13; "comprises a partial sequence of 50 to 350 amino acids of the polypeptide" of SEQ ID NO:2 SEQ ID NO:4 or SEQ ID NO:6 of claim 21; which comprises "amino acids 1-200 of the polypeptide" or "amino acids 185-500 of the polypeptide" of SEQ ID NO:2 SEQ ID NO:4 or SEQ ID NO:6 of claim 22; which "comprises (a) a polypeptide which is encoded by single nucleotide polymorph of a polynucleotide whose sequence is set forth in SEQ ID NO: 1, (b) a single amino acid polymorph of a polypeptide whose sequence is set forth in SEQ ID NO: 2" of claim 33 is inherent. The reference Phl p 4 molecule is the same as the protein of claims. Further characterization of a known compound does not make it patentably distinct. See Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999) "Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art... However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. " The Court further held that "this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art."

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It is noted in the specification on page 14 that there are three natural isoforms of the heterogenous Phl p 4 allergen molecule (SEQ ID NOs 2, 4 and 6). Since the office does not have a laboratory to test the reference Phl p 4 allergen, it is applicant's burden to show that the reference allergen does not comprise the amino acid sequences of SEQ ID NO:2, 4 and 6 recited

in the claims. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980).

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Contrary to Applicant's assertion, Fahlbusch et al. need not teach the polypeptide sequence to anticipate the instant claims. Further characterization of a known compound does not make it patentably distinct. See Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999) "Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art... However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. " The Court further held that "this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art." Therefore, it is Applicant's burden to prove that the reference Phl p 4 molecule, which was isolated from the same source as the claimed Phl p 4 allergen, does not have the sequence of SEQ ID NO:2, 4 or 6. Where the Patent Office has reason to believe that a functional limitation

asserted to be critical for establishing novelty in the claimed subject matter may be an inherent characteristic of the prior art, it has the authority to require the applicant to prove that the subject matter shown in the prior art does not possess the characteristics relied on. In re Schreiber, 44 USPQ2d 1429 (Fed. Cir. 1997).

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

September 21, 2009
Nora M. Rooney
Patent Examiner
Technology Center 1600

/Nora M Rooney/

Examiner, Art Unit 1644